

**EXAMINER'S AMENDMENT**

1. Claims 33-34 have been cancelled and claims 35 and 38 have been amended as requested in the amendment filed on November 19, 2003. Claims 1-32 and 35-51 are pending in the instant application.

Claims 1-32 and 39-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Claims 35-38 are under examination in the instant office action.

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Gregory B. Butler on March 26, 2004.

The application has been amended as follows:

Cancel claims 1-32 and 39-51.

Amend claims 35 and 36 as follows:

1 ~~35.~~ (currently amended) A composition comprising Mg<sup>2+</sup> and at least one peptide selected from the group consisting of: WRQTRKD (SEQ ID NO: 1); HYAKNPI (SEQ ID NO: 2); ATINKSL (SEQ ID NO: 3); RRRGMAI (SEQ ID NO: 4); ~~THRLPSR (SEQ ID NO: 5);~~ TKHGPRK (SEQ ID NO: 6); SLKRLPK (SEQ ID NO: 7); RLRGRNQ (SEQ ID NO: 8);

WPFHHHR (SEQ ID NO: 9); HLYHHKT (SEQ ID NO: 10); THIHHPS (SEQ ID NO: 11); and  
MMMMMMRL (SEQ ID NO: 12). <sup>1</sup>

2 ~~36.~~ (currently amended) The composition of claim ~~35~~, wherein the peptide is selected from  
the group consisting of: ~~THRLPSR (SEQ ID NO: 5)~~; SLKRLPK (SEQ ID NO: 7); THIHHPS  
(SEQ ID NO: 11); and MMMMMRL (SEQ ID NO: 12).

3. Claims 35-38 are allowed. Claims 35-38 are renumbered as 1-4, respectively.

4. The prior art made of record and not relied upon is considered pertinent to applicant's  
disclosure:

Turnbough, WO 99/36081 (22 July, 1999); Turnbough, Pub. No.: US 2003/0044838 A1,  
March 06, 2003, filing date January 14, 1999.

Copies of the sequence alignments are attached to the instant office action.

Any inquiry concerning this communication or earlier communications from the  
examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870.  
The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's  
supervisor, Yvonne Eyler can be reached on (571) 272-0871. The fax phone number for the  
organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600  
by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax  
center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices  
published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December

28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

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Olga N. Chernyshev, Ph.D.

**Amendments to the Claims:**

This listing of claims will replace all prior versions of the same numbered claims in the application:

**Listing of claims:**

1. (withdrawn) A method for determining whether an agent is capable of inhibiting the aggregation of  $\alpha$ , comprising:

(a) adding said agent to a sample containing  $\alpha$ -synuclein in the presence of exogenous iron or copper, and allowing the  $\alpha$ -synuclein to aggregate;

(b) determining the amount, if any, of aggregated  $\alpha$ -synuclein; and

(c) comparing the amount from step (b) with an amount determined in a control sample wherein said agent is absent,

wherein a decrease in the amount of aggregated  $\alpha$ -synuclein indicates that the agent is capable of inhibiting the aggregation of  $\alpha$ -synuclein.

2. (withdrawn) The method of claim 1, wherein free radical generator(s) is added to the sample in step (a) to assist in the aggregation of  $\alpha$ -synuclein.

3. (withdrawn) The method of claim 1, wherein in step (a) exogenous iron is added.

4. (withdrawn) The method of claim 2, wherein the free radical generator is dopamine or hydrogen peroxide.

5. (withdrawn) The method of claim 1, wherein the sample is composed of cells that over-express  $\alpha$ -synuclein.

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6. (withdrawn) The method of claim 5, wherein the cells are of neuronal origin.
7. (withdrawn) The method of claim 1, wherein the amount of aggregation is determined by protein separation, whereby the aggregated material displays a higher molecular weight than unaggregated  $\alpha$ -synuclein.
8. The method of claim 7, wherein the protein separation is accomplished by gel electrophoresis.
9. (withdrawn) The method of claim 1, wherein the amount of aggregation is determined by adding a labeled anti-  $\alpha$ -synuclein antibody and measuring the bound label.
10. (withdrawn) The method of claim 9, wherein the label is a peroxidase.
11. (withdrawn) The method of claim 1, wherein the amount of aggregation is determined by binding to thioflavine-S.
12. (withdrawn) A kit for testing affects of substances on aggregation of  $\alpha$ -synuclein, comprising lyophilized  $\alpha$ -synuclein, iron or copper salt, and a buffer.
13. (withdrawn) The kit of claim 12, which comprises iron chloride.
14. (withdrawn) The kit of claim 12, which further comprises a free radical generator.
15. (withdrawn) The kit of claim 14, wherein the free radical generator is hydrogen peroxide.
16. (withdrawn) A method for treating a neurodegenerative disease that involves the formation of Lewy bodies, comprising administering to a patient in need thereof one or more agents that inhibit the formation of  $\alpha$ -synuclein

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aggregates, whereby the presence of Lewy bodies remains the same or is reduced.

17. (withdrawn) The method of claim 16, wherein the agent is Mg<sup>2+</sup>.
18. (withdrawn) The method of claim 17, wherein the agent is MgSO<sub>4</sub>.
19. (withdrawn) The method of claim 16, wherein the agent is a peptide that binds to  $\alpha$ -synuclein and inhibits the aggregation thereof.
20. (withdrawn) The method of claim 19, wherein said peptide binds to any part of the C-terminal amino acids 113 - 140, or the NAC (non-amyloid- $\beta$  protein component) portion of  $\alpha$ -synuclein.
21. (withdrawn) The method of claim 20, wherein the peptide is selected from the group consisting of: WRQTRKD; HYAKNPI; ATINKSL; RRRGMAI; THRLPSR; TKHGPRK; SLKRLPK; RLRGRNQ; WPFHHHR; HLYHHKT; THIHHPS; and MMMMMRLL.
22. (withdrawn) The method of claim 21, wherein the peptide is selected from the group consisting of: THRLPSR; SLKRLPK; THIHHPS; and MMMMMRLL.
23. (withdrawn) The method of claim 22, wherein the peptide is SLKRLPK.
24. (withdrawn) The method of claim 16, wherein the agent is a composition containing Mg<sup>2+</sup> in combination with a peptide.
25. (withdrawn) The method of claim 24, wherein the agent is selected from the group consisting of: WRQTRKD; HYAKNPI; ATINKSL; RRRGMAI; THRLPSR; TKHGPRK; SLKRLPK; RLRGRNQ; WPFHHHR; HLYHHKT; THIHHPS; and MMMMMRLL.

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26. (withdrawn) The method of claim 25, wherein the agent is selected from the group consisting of: THRLPSR; SLKRLPK; THIHHPS; and MMMMMR.

27. (withdrawn) The method of claim 26, wherein the peptide is SLKRLPK.

28. (withdrawn) The method of claim 16, wherein the neurodegenerative disease is Parkinson's disease, Alzheimer's disease diffuse Lewy body disease, mixed AD-PD, multiple system atrophy and Hallervorden-Spatz disease.

29. (withdrawn) The method of claim 28, wherein the neurodegenerative disease is Parkinson's disease.

30. (withdrawn) A method for inhibiting the formation of aggregates of  $\alpha$ -synuclein, comprising treating the  $\alpha$ -synuclein with a substance containing  $Mg^{2+}$ .

31. (withdrawn) A method for inhibiting the formation of aggregates of  $\alpha$ -synuclein, comprising treating the  $\alpha$ -synuclein with a peptide that binds to  $\alpha$ -synuclein and inhibits the aggregation thereof.

32. (withdrawn) The method of claim 30, wherein the substance further comprises at least one peptide that binds to  $\alpha$ -synuclein and inhibits the aggregation thereof.

33. (canceled) The composition comprising  $Mg^{2+}$  and at least one peptide which binds  $\alpha$ -synuclein and inhibits the aggregation thereof.

34. (canceled) The composition of claim 33, wherein the peptide binds the C-terminal or the NAC portion of  $\alpha$ -synuclein.

35. (currently amended) AThe composition comprising  $Mg^{2+}$  and at least one peptide of claim 34, wherein the peptide is selected from the group consisting of: WRQTRKD (SEQ ID NO: 1); HYAKNPI (SEQ ID NO: 2); ATINKSL (SEQ ID NO: 3);

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RRRGMAI (SEQ ID NO: 4); THRLPSR (SEQ ID NO: 5); TKHGPRK (SEQ ID NO: 6); SLKRLPK (SEQ ID NO: 7); RLRGRNQ (SEQ ID NO: 8); WPFHHHR (SEQ ID NO: 9); HLYHHKT (SEQ ID NO: 10); THIHHPS (SEQ ID NO: 11); and MMMMMRL (SEQ ID NO: 12).

36. (previously amended) The composition of claim 35, wherein the peptide is selected from the group consisting of: THRLPSR (SEQ ID NO: 5); SLKRLPK (SEQ ID NO: 7); THIHHPS (SEQ ID NO: 11); and MMMMMRL (SEQ ID NO: 12).

~~3~~ <sup>2</sup> 37. (previously amended) The composition of claim ~~36~~<sup>2</sup>, wherein the peptide is SLKRLPK (SEQ ID NO: 7).

~~4~~ <sup>1</sup> 38. (currently amended) The composition of claim ~~35~~<sup>1</sup>, wherein Mg<sup>2+</sup> is MgSO<sub>4</sub>.

39. (withdrawn) A peptide that will bind to  $\alpha$ -synuclein and inhibit its aggregation.

40. (withdrawn) The peptide of claim 39, wherein the peptide comprises a sequence selected from the group consisting of: WRQTRKD; HYAKNPI; ATINKSL; RRRGMAI; THRLPSR; TKHGPRK; SLKRLPK; RLRGRNQ; WPFHHHR; HLYHHKT; THIHHPS; and MMMMMRL.

41. (withdrawn) The peptide of claim 40, wherein the peptide comprises a sequence selected from the group consisting of: THRLPSR; SLKRLPK; THIHHPS; and MMMMMRL.

42. (withdrawn) The peptide of claim 41, which comprises the sequence SLKRLPK.

43. (withdrawn) A composition comprising the peptide of claim 39, and a pharmaceutically acceptable carrier.

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44. (withdrawn) The composition of claim 43, which comprises a peptide containing a sequence selected from the group consisting of: WRQTRKD; HYAKNPI; ATINKSL; RRRGMAI; THRLPSR; TKHGPRK; SLKRLPK; RLRGRNQ; WPFHHHR; HLYHHKT; THIHHPS; and MMMMMRRL.

45. (withdrawn) The composition of claim 44, which comprises a peptide containing a sequence selected from the group consisting of: THRLPSR; SLKRLPK; THIHHPS; and MMMMMRRL.

46. (withdrawn) The composition of claim 45, which comprises a peptide containing the sequence SLKRLPK.

47. (withdrawn) A method for identifying peptides that are useful for inhibiting the aggregation of  $\alpha$ -synuclein, comprising:

- a) binding an  $\alpha$ -synuclein C-terminal or NAC portion peptide to a solid substrate;
- (b) adding a phage display library of random peptides, and allowing binding to take place with the  $\alpha$ -synuclein;
- (c) detecting any bound phage; and
- (d) determining which peptide is displayed on bound phage, whereby such a peptide is useful for inhibiting aggregation of  $\alpha$ -synuclein.

48. (withdrawn) The method of claim 47, wherein the  $\alpha$ -synuclein peptide contains amino acids 121 - 131 of  $\alpha$ -synuclein.

49. (withdrawn) The method of claim 47, wherein the  $\alpha$ -synuclein peptide contains amino acids 61-87 of  $\alpha$ -synuclein.

50. (withdrawn) The method of claim 47, wherein the peptides of the phage display library are seven amino acids in length.

51. (withdrawn) A method for determining whether an agent is capable of inhibiting the aggregation of  $\alpha$ -synuclein, comprising:

- (a) labelling  $\alpha$ -synuclein with a fluorescent label, and mixing labelled and unlabelled  $\alpha$ -synuclein in solution with an agent suspected of being inhibitory to  $\alpha$ -synuclein aggregation, and allowing the  $\alpha$ -synuclein to aggregate;
- (b) determining the amount, if any, of aggregation of  $\alpha$ -synuclein by monitoring changes in the anisotropy of the solution by observing changes in the polarization of the solution; and
- (c) comparing the amount from step (b) with an amount determined in a control sample wherein said agent is absent, wherein changes in the polarization indicate aggregation has occurred, and whererin an observed decrease in the amount of aggregation in the presence of the agent indicates that the agent is capable of inhibiting the aggregation of  $\alpha$ -synuclein.